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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

LI ET AL.

APPLICATION NO:

FILED: MARCH 23, 2004

FOR: MICROBIAL TRANSFORMATION METHOD FOR THE
PREPARATION OF AN EPOTHILONE

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

This paper is being filed within three months of the filing date of the application. Therefore, no fees are required. If a fee is deemed to be required, the Commissioner is hereby authorized to charge such fee to Deposit Account No. 19-3880.

In accordance with 37 C.F.R. §1.56, applicants wish to call the Examiner's attention to the references cited on the attached form(s) PTO-1449.

Some of the listed references are of record in parent Application No. 09/468,854 filed December 21, 1999, and copies are available therein. However, applicants are willing to send copies of any or all of these references at the Examiner's request.

Also, copies of the other cited references are enclosed herewith.

REMARKS

Claims 4, 7, and 11 have been amended to correct the structure for the group G₂. The corrected structure has a methyl group as a substituent to the thiazole ring.

Support for this amendment is found in the specification in Example 1.

As such, no new matter has been entered.


Conclusion

The Examiner is invited to contact the undersigned if it is believed a telephonic communication would expedite the prosecution of this application.

In the event that the Commissioner determines any extra fee to be due, please charge any necessary additional fees (or credit any overpayment) to the Assignee's Deposit Account No. 19-3880.

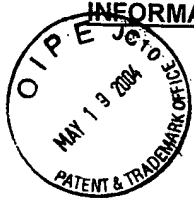
Respectfully submitted,

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Agent for Applicants
Reg. No. 47,609

Date: May 19, 2004



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Docket No.: LD154 DIV1 Sheet 1 of 7

Serial No.: 10/807089 Group:

Applicant: Wenying Li et al.

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U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-class	Filing Date
	AA	08/856,533	5/14/97	Nicolaou, K., et al.			5/14/97
	AB	08/923,869	9/4/97	Nicolaou, K., et al.			9/4/97
	AC	60/032,864	12/13/96	Nicolaou, K., et al.			12/13/96

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	BA	4138042.8	5/27/93	Germany (German and English abstract)			
	BB	19639456.2	5/29/97	Germany (German and English translation)			
	BC	19542986.9	5/29/97	Germany (German and English translation)			
	BD	19636343.8	3/5/98	Germany (German and English abstract)			
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	BF	19645362.3	4/30/98	Germany (German and English abstract)			
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	BH	19701758	7/23/98	Germany (German and English abstract)			
	BI	19707505.3	9/3/98	Germany (German and English abstract)			
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	BK	19720312	11/19/98	Germany (German and English abstract)			
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	BM	879 605	11/25/98	Europe (German and English abstract)			
	BN	19726627	12/24/98	Germany (German and English abstract)			
	BO	93/10121	5/27/93	World (PCT as published and English abstract)			
	BP	97/19086	5/29/97	World (PCT as published and English translation)			
	BQ	98/08849	3/5/98	World (PCT as published and English abstract)			
	BR	98/22461	5/28/98	World (PCT as published and English translation)			
	BS	98/24427	6/11/98	World			

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	BT	98/25929	6/18/98	World (PCT as published and priority documents: U.S. 60/032,864, 08/856,533, 08/923,869)			
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	BV	98/47891	10/29/98	World (PCT as published and English abstract)			
	BW	99/01124	1/14/99	World			
	BX	99/03848	1/28/99	World (PCT as published and English abstract)			
	BY	99/07692	2/18/99	World (PCT as published and English translation)			

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	CA	Balog, A., et al., "Total Synthesis of (-)-Epothilone A", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 35, No. 23/24, 2801-2803 (1996)
	CB	Bertini, F., et al., "Alkenes from Epoxides by Reductive Elimination with Magnesium Bromide-Magnesium Amalgam", <i>Chem. Commun.</i> , 144 (1970)
	CC	Bollag, D.M., et al., "Epothilones, A New Class of Microtubule-stabilizing Agents with a Taxol-like Mechanism of Action", <i>Cancer Res.</i> 55, No. 11, 2325-2333 (1995)
	CD	Fujisawa, T., et al., "Deoxygenation of Epoxides to Olefins with FeCl ₃ - n-BuLi System", <i>Chem. Lett.</i> , 883-886 (1974)
	CE	Fujiwara, Y., et al., "Reductive Coupling of Carbonyl Compounds to Olefins by Tungsten Hexachloride-Lithium Aluminum Hydride and Some Tungsten and Molybdenum Carbonyls", <i>J. Org. Chem.</i> , Vol. 43, No. 12, 2477-2479 (1978)
	CF	Gladysz, J. A., et al., "Deoxygenation of Epoxides by Metal Atom Cocondensation", <i>J. Org. Chem.</i> , Vol. 41, No. 22, 3647-3648 (1976)
	CG	Hofle, G., et al., "Epothilone A and B - Novel 16-Membered Macrolides with Cytotoxic Activity: Isolation, Crystal Structure, and Conformation in Solution", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 35, No. 13/14, 1567-1569 (1996)
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CK	Kupchan, S. M., et al., "Reductive Elimination of Epoxides to Olefins with Zinc-Copper Couple", <i>J. Org. Chem.</i> , Vol. 36, No. 9, 1187-1190 (1971)
CL	Martin, M. G., et al., "Epoxides as Alkene Protecting Groups. A Mild and Efficient Deoxygenation", <i>Tetrahedron Letters</i> , Vol. 25, No. 3, 251-254 (1984)
CM	McMurry, J. E., et al., "Reduction of Epoxides to Olefins with Low Valent Titanium", <i>J. Org. Chem.</i> , Vol. 40, No. 17, 2555-2556 (1975)
CN	McMurry, J. E., et al., "Some Deoxygenation Reactions with Low-Valent Titanium (TiCl ₃ /LiAlH ₄)", <i>J. Org. Chem.</i> , Vol. 43, No. 17, 3249-3254 (1978)
CO	Meng, D., et al., "Remote Effects in Macrolide Formation Through Ring-Forming Olefin Metathesis: An Application to the Synthesis of Fully Active Epothilone Congeners", <i>J. Am. Chem. Soc.</i> , Vol. 119, No. 11, 2733-2734 (1997)
CP	Nicolaou, K. C., et al., "An Approach to Epothilones Based on Olefin Metathesis", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 35, No. 20, 2399-2401 (1996)
CQ	Nicolaou, K. C., et al., "Total Synthesis of Epothilone A: The Macrolactonization Approach", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 36, No. 5, 525-527 (1997)
CR	Nicolaou, K. C., et al., "Designed Epothilones: Combinatorial Synthesis, Tubulin Assembly Properties, and Cytotoxic Action against Taxol-Resistant Tumor Cells", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 36, No. 19, 2097-2103 (1997)
CS	Nicolaou, K. C., et al., "The Olefin Metathesis Approach to Epothilone A and Its Analogues", <i>J. Am. Chem. Soc.</i> , Vol. 119, No. 34, 7960-7973 (1997)
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CU	Nicolaou, K. C., et al., "Synthesis of Epothilones A and B in Solid and Solution Phase", <i>Nature</i> , Vol. 387, 268-272 (1997)
CV	Nicolaou, K. C., et al., "Synthesis of Epothilones A and B in Solid and Solution Phase" (Correction to <i>Nature</i> 387, 268-272 (1997)), <i>Nature</i> , 390, 100 (1997)
CW	Raucher, S., et al., "Total Synthesis of (+)-Dihydrocostunolide via Tandem Cope-Claisen Rearrangement", <i>J. Org. Chem.</i> , Vol. 51, No. 26, 5503-5505 (1986)
CX	Sato, M., et al., "Reduction of Organic Compounds with Low-Valent

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CAB	Su, D.-S., et al., "Total Synthesis of (-)-Epothilone B: An Extension of the Suzuki Coupling Method and Insights into Structure-Activity Relationships of the Epothilones", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 36, No. 7, 757-759 (1997)
CAC	Su, D.-S., et al., "Structure-Activity Relationships of the Epothilones and the First In Vivo Comparison with Paclitaxel", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 36, No. 19, 2093-2096 (1997)
CAD	Victory, S. F., et al., "Relative Stereochemistry and Solution Conformation of the Novel Paclitaxel-Like Antimitotic Agent Epothilone A", <i>Bioorg. Med. Chem. Letts.</i> , Vol. 6., No. 7, 893-898 (1996)
CAE	Winkler, J. D., et al., "A Model For The Taxol (Paclitaxel)/Epothilone Pharmacophore", <i>Bioorg. Med. Chem. Letts.</i> , Vol. 6, No. 24, 2963-2966 (1996)
CAF	Yang, Z., et al., "Total Synthesis of Epothilone A: The Olefin Metathesis Approach", <i>Angew. Chem. Int. Ed. Engl.</i> , Vol. 36, No. 1 / 2, 166-168 (1997)
CAG	Bollag, D., et al., "Epothilone, A New Structural Class of Microtubule Stabilizer", Abstract, <i>Proc. Am. Assoc. Cancer Res.</i> , Vol. 36, 86 Meet. 454 (1995)
CAH	Bollag, D., "Epothilones: Novel Microtubule-Stabilising Agents", <i>Expert Opin. Invest. Drugs</i> , Vol. 6, No. 7, 867-873 (1997)
CAI	Bertinato, P., et al., "Studies Toward a Synthesis of Epothilone A: Stereocontrolled Assembly of the Acyl Region and Models for Macrocyclization", <i>J. Org. Chem.</i> , Vol. 61, No. 23, 8000-8001 (1996)
CAJ	<i>Chemical & Engineering News</i> , "Epothilone Epiphany: Total Syntheses", Vol. 74, No. 52, 24-26 (1996)
CAK	<i>Chemical & Engineering News</i> , "First Total Synthesis of Epothilone B", Vol. 75, No. 13, 23 (1997)
CAL	<i>Chemical & Engineering News</i> , "Solid-Phase Epothilone Synthesis Used to Create Analog Library", Vol. 75, No. 20, 33 (1997)
CAM	Claus, E., et al., "Synthesis of the C1-C9 Segment of Epothilons", <i>Tetrahedron Lett.</i> , Vol. 38, No. 8, 1359-1362 (1997)
CAN	De Brabander, J., et al., "Towards a Synthesis of Epothilone A: Rapid Assembly of the C1-C6 and C7-C12 Fragments", <i>Synlett</i> , Vol. 7, 824-826 (1997)
CAO	Gabriel, T. and Wessjohann, L., "The Chromium-Reformatsky Reaction: Asymmetric Synthesis of the Aldol Fragment of the Cytotoxic Epothilons from 3-(2-Bromoacyl)-2-Oxazolidinones", <i>Tetrahedron Lett.</i> , Vol. 38, No.

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Serial No.: 10/807089 Group:

Applicant: Wenying Li et al.

Filing Date: March 23, 2004

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	CAQ	Marshall, A., "Total Synthesis of Epothilone", <i>Nature Biotechnology</i> , Vol. 15, No. 3, 205 (1997)
	CAR	Meng, D., et al., "Studies Toward a Synthesis of Epothilone A: Use of Hydropyran Templates for the Management of Acyclic Stereochemical Relationships", <i>J. Org. Chem.</i> , Vol. 61, No. 23, 7998-7999 (1996)
	CAS	Meng, D., et al., "Total Syntheses of Epothilones A and B", <i>J. Am. Chem. Soc.</i> , Vol. 119, No. 42, 10073-10092 (1997)
	CAT	Mensching, S. and Kalesse, M., "Generation of Thiazoles by Column Dehydrogenation of Thiazolidines with MnO ₂ ", <i>J. Prakt. Chem.</i> , Vol. 339, No. 1, 96-97 (1997)
	CAU	Mulzer, J. and Mantoulidis, A., "Synthesis of the C(1)-C(9) Segment of the Cytotoxic Macrolides Epothilone A and B", <i>Tetrahedron Lett.</i> , Vol. 37, No. 51, 9179-9182 (1996)
	CAV	Nicolaou, K., et al., "Chemistry, Biology and Medicine of Selected Tubulin Polymerizing Agents", <i>Pure Appl. Chem.</i> , Vol. 71, No. 6, 989-997 (1999)
	CAW	Nicolaou, K., et al., "Total Synthesis of Epothilone E and Related Side-chain Modified Analogues Via a Stille Coupling Based Strategy", <i>Bioorg. Med. Chem.</i> , Vol. 7, No. 5, 665-697 (1999)
	CAX	Schinzer, D., et al., "Studies Towards the Total Synthesis of Epothilones: Asymmetric Synthesis of the Key Fragments", <i>Chem. Eur. J.</i> , Vol. 2, No. 22, 1477-1482 (1996)
	CAY	Taylor, R. and Haley, J., "Towards the Synthesis of Epothilone A: Enantioselective Preparation of the Thiazole Sidechain and Macrocyclic Ring Closure", <i>Tetrahedron Lett.</i> , Vol. 38, No. 12, 2061-2064 (1997)
	CAZ	Schinzer, D., et al., "Syntheses of (-)-Epothilone A", <i>Chem. Eur. J.</i> , Vol. 5, No. 9, 2483-2491 (1999)
	CBA	Schinzer, D., et al., "Syntheses of (-)-Epothilone B", <i>Chem. Eur. J.</i> , Vol. 5, No. 9, 2492-2500 (1999)
	CBB	Nicolaou, K. C., et al., "Synthesis and Biological Properties of C12,13-Cyclopropylepothilone A and Related Epothilones", <i>Chemistry & Biology</i> , Vol. 5, No. 7, 365-372 (1998)

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U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-class	Filing Date
	AD	6,605,599	08/12/03	Vite et al.			
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FOREIGN PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Country	Class	Sub-class	Filing Date
	00/31246	2/6/00	PCT			
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	CBC	U. Bornscheuer, Biotechnology and Bioengineering, Vol. 58, No. 5, pages 554-559, 1998
	CBD	Nicolaou et al., "Total Synthesis of 26-Hydroxyepothilone B and Related Analogues", Chem. Commun., 24, 2343-2344 (1997)
	CBE	Nicolaou et al., "Total Synthesis of 26-Hydroxy-Epothilone B and Related Analogs Via a Macrolactonization Based Strategy", Tetrahedron, 54, 7127-7166 (1998)